RECOMBINANT MODEIFIED VACCINIA VIRUS ANKARA (MVA) EXPRESSING MULTIVALENT TUBERCULOSIS ANTIGENS PROVIDING PROTECTION AGAINST MYCOBACTERIUM TUBERCULOSIS.

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Recombinants based on the attenuated modified vaccinia virus Ankara (MVA) strain have been used widely as foreign gene delivery systems to study many biological functions of target genes and as vaccines against many pathogens, particularly in the scientific and clinical field. Here we established a promising new vaccine candidate the multivalent recombinant MVA tuberculosis vaccine (multi-rTB MVA), which is a leading candidate vaccine designed to boost the protective efficacy of BCG. Testing the protection obtained from a new vaccine candidate using the guinea pig model has been demonstrated against *Mycobacterium tuberculosis* (mtb) inoculation, and the toxic response generated. To identify the immunological surrogate markers for the development of a protective immune response against mtb challenge, we analyzed immune response after priming or prime-boosting by using cytoplasmic cytokine detecting and assays for cytokine secretion in guinea pigs. Collectively, our findings indicate the following: (i) multi-rTB MVA containing novel TB genes encoding 30-kDa antigen complex, 25-kDa membrane protein, 40-kDa phosphate transporters homologous, and 6-kDa early secreted antigen target protein were effective molecules for inducing protective immunity against tuberculosis in vaccinated animal models. (ii) The multi-rTB MVA-immunized animals were significantly better protected against mtb than animals immunized with the parental strain of BCG. (iii) Seven days after vaccination, guinea pig vaccinated with multi-rTB MVA were found to have significantly higher Th1-polarized IFN-γ concentrations than animal in the untreated controls. The frequencies of IL-2, IFN-γ, and TNF-α producing cell were demonstrated higher than controls by flow cytometry of CD4-gated cells. Boosting with the multi-rTB MVA, but not priming with tice BCG, greatly increased the mtb antigens-specific CD4 + and CD8 + T-cell response, suggesting that the mechanism of protection may differ from that against BCG. Conceivably, multi-rTB MVA vaccination capable of inducing efficient cell-mediated immunity might be used as an effective vaccine for tuberculosis.